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Preliminary Amendment -1showing changes for
§ 371 Patent Application of PCT/EP00/02410
Markl, et al.
filed September 17, 2001

- 1. Nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:
- (b) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

```
SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtHl domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
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   SEQ ID NO:19 (partial KLH1 domain e),
  SEQ ID NO:20 (KLH2 domain b),
  SEQ ID NO:21 (KLH2 domain c),
  SEQ ID NO:22 (partial KLH2 domain d),
  SEQ ID NO:23 (KLH2 domain g),
  SEQ ID NO:24 (partial KLH2 domain h),
  SEQ ID NO:49 (HtH1 domain a' + signal peptide),
  SEQ ID NO:50 (partial HtH2 domain a),
  SEQ ID NO:51 (HtH2 domain b'),
  SEQ ID NO:52 (HtH2 domain d'),
  SEQ ID NO:53 (HtH2 domain e'),
  SEQ ID NO:54 (KLH1 domain e'),
  SEQ ID NO:55 (KLH1 domain f),
  SEQ ID NO:56 (KLH1 domain g),
  SEQ ID NO:57 (KLH2 domain b'),
  SEQ ID NO:58 (KLH2 domain c'),
  SEQ ID NO:59 (KLH2 domain d'),
  SEQ ID NO:60 (KLH2 domain e),
  SEQ ID NO:61 (KLH2 domain f),
  SEQ ID NO:62 (KLH2 domain g'),
  SEQ ID NO:80 (HtH1 domain a" + signal peptide),
  SEQ ID NO:81 (HtH1 domain b"),
  SEQ ID NO:82 (HtH1 domain c"),
  SEQ ID NO:83 (HtH1 domain d"),
  SEQ ID NO:84 (HtH1 domain e"),
  SEQ ID NO:85 (HtH1 domain f"),
  SEQ ID NO:86 (HtH1 domain g"),
  SEQ ID NO:87 (HtH1 domain h"),
  SEQ ID NO:88 (partial HtH2 domain a"),
  SEQ ID NO:89 (HtH2 domain b"),
  SEQ ID NO:90 (HtH2 domain c"),
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Preliminary Amendment -3showing changes for § 371 Patent Application of PCT/EP00/02410 Markl, et al. filed September 17, 2001 SEQ ID NO:91 (HtH2 domain d"), SEQ ID NO:92 (HtH2 domain e"), SEQ ID NO:93 (HtH2 domain f"), SEQ ID NO:94 (HtH2 domain g"), SEQ ID NO:95 (HtH2 domain h"), SEQ ID NO:96 (partial KLH1 domain b"), SEQ ID NO:97 (KLH1 domain c"), SEQ ID NO:98 (KLH1 domain d"), SEQ ID NO:99 (KLH1 domain e"), SEQ ID NO:100 (KLH1 domain f"), SEQ ID NO:101 (KLH1 domain g"), SEQ ID NO:102 (KLH2 domain b"), SEQ ID NO:103 (KLH2 domain c"), SEQ ID NO:104 (KLH2 domain d"), SEQ ID NO:105 (KLH2 domain e"), SEQ ID NO:106 (KLH2 domain f"), SEQ ID NO:107 (KLH2 domain g"), SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one

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of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;

- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences described under (a) to (f).
- 2. Nucleic acid molecule according to claim 1, characterized in that the hybridization described under (b) or (d) is carried out under stringent conditions.
- 3. Nucleic acid molecule according to claim 1, characterized in that the nucleic acid molecule described under (e) is at least 80% homologous to one of the nucleic acid sequences described under (a).
- 4. Nucleic acid molecule according to claim 1,

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characterized in that the nucleic acid molecule described under (e) is at least 90 % homologous to one of the nucleic acid sequences described under (a).

- 5. Nucleic acid molecule according to claim 1, characterized in that the nucleic acid molecule described under (e) is at least 95 % homologous to one of the nucleic acid sequences described under (a).
- 6. Nucleic acid molecule according to one of claims 1-to 5, characterized in that it is a deoxyribonucleic acid molecule.
- 7. Construct comprising a nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:
- (b) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),

SEQ ID NO:2 (HtH1 domain b),

SEQ ID NO:3 (HtH1 domain c),

SEQ ID NO:4 (HtH1 domain d),

```
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
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SEQ ID NO:59 (KLH2 domain d'),

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SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtHl domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtHl domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
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SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and

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- (g) combinations of several of the DNA sequences

 described under (a) to (f)

 according to one of claims 1 to 6.
- 8. Construct according to claim 7, furthermore comprising a promoter which is suitable for expression control, the nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof being under the control of the promoter.
- 9. Construct according to claim 7—or—8, furthermore comprising a nucleic acid sequence which codes for an antigen and is coupled directly to the nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof.
- 10. Construct according to claim 9, wherein the antigen is selected from: _tumour antigens, virus antigens and antigens of bacterial or parasitic pathogens.
- 11. Construct according to one of claims 7—to 10, wherein the construct comprises at least a part of a vector, the vector being selected from: bacteriophages, adenoviruses, vaccinia viruses, baculoviruses, SV40 virus and retroviruses.
- 12. Construct according to one of claims 7—to 11, wherein the construct furthermore comprises a His tag-coding nucleic acid sequence and the expression

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of the construct leads to the formation of a fusion protein with a His tag.

- 13. Host cell containing a construct—according to one of claims 7 to 12, wherein the host cell is a prokaryotic or eukaryotic cell suitable for expression of the construct and wherein said construct comprises a nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:
- (b) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

```
SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
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SEQ ID NO:3 (HtH1 domain c),

SEQ ID NO:4 (HtHl domain d),

SEQ ID NO:5 (HtH1 domain e),

SEQ ID NO:6 (HtH1 domain f),

SEQ ID NO:7 (HtH1 domain g),

SEQ ID NO: 8 (HtH1 domain h),

SEQ ID NO:9 (partial HtH2 domain b),

SEQ ID NO:10 (HtH2 domain c),

SEQ ID NO:11 (HtH2 domain d),

SEQ ID NO:12 (HtH2 domain e),

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SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
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SEQ ID NO:84 (HtH1 domain e"),

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SEQ ID NO:85 (HtH1 domain f"), SEQ ID NO:86 (HtH1 domain g"), SEQ ID NO:87 (HtH1 domain h"), SEQ ID NO:88 (partial HtH2 domain a"), SEQ ID NO:89 (HtH2 domain b"), SEQ ID NO:90 (HtH2 domain c"), SEQ ID NO:91 (HtH2 domain d"), SEQ ID NO:92 (HtH2 domain e"), SEQ ID NO:93 (HtH2 domain f"), SEQ ID NO:94 (HtH2 domain g"), SEQ ID NO:95 (HtH2 domain h"), SEQ ID NO:96 (partial KLH1 domain b"), SEQ ID NO:97 (KLH1 domain c"), SEQ ID NO:98 (KLH1 domain d"), SEQ ID NO:99 (KLH1 domain e"), SEQ ID NO:100 (KLH1 domain f"), SEQ ID NO:101 (KLH1 domain g"), SEQ ID NO:102 (KLH2 domain b"), SEQ ID NO:103 (KLH2 domain c"), SEQ ID NO:104 (KLH2 domain d"), SEQ ID NO:105 (KLH2 domain e"), SEQ ID NO:106 (KLH2 domain f"), SEQ ID NO:107 (KLH2 domain g"), SEQ ID NO:108 (partial KLH2 domain h");

(b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;

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- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one
 of the nucleic acid sequences described under (a)
 to (c) and the counter-strand of which codes for a
 polypeptide which has the immunological properties
 of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences described under (a) to (f).
- 14. Host cell according to claim 13, characterized in that the prokaryotic host cell is selected from E. coli and Bacillus subtilis.

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- 15. Host cell according to claim 13, characterized in that the eukaryotic host cell is selected from yeast cells, plant cells, insect cells and mammalian cells, preferably from CHO cells, COS cells and HeLa cells.
- 16. Process for the preparation of a haemocyanin polypeptide, wherein athe nucleic acid molecule according to one of claims 1 to 6 and/or athe construct comprising said nucleic acid moleculeaccording to one of claims 7 to 12 is expressed in a suitable host cell and the protein is isolated, if appropriate, wherein said nucleic acid molecule comprising a nucleic acid molecule comprises a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:
- (b) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),

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SEQ ID NO:7 (HtH1 domain g), SEQ ID NO: 8 (HtH1 domain h), SEQ ID NO:9 (partial HtH2 domain b), SEQ ID NO:10 (HtH2 domain c), SEQ ID NO:11 (HtH2 domain d), SEQ ID NO:12 (HtH2 domain e), SEQ ID NO:13 (HtH2 domain f), SEQ ID NO:14 (HtH2 domain g), SEQ ID NO:15 (HtH2 domain h), SEQ ID NO:16 (partial KLH1 domain b), SEQ ID NO:17 (KLH1 domain c), SEQ ID NO:18 (KLH1 domain d), SEQ ID NO:19 (partial KLH1 domain e), SEQ ID NO:20 (KLH2 domain b), SEQ ID NO:21 (KLH2 domain c), SEQ ID NO:22 (partial KLH2 domain d), SEQ ID NO:23 (KLH2 domain g), SEQ ID NO:24 (partial KLH2 domain h), SEQ ID NO:49 (HtHl domain a' + signal peptide), SEQ ID NO:50 (partial HtH2 domain a), SEQ ID NO:51 (HtH2 domain b'), SEQ ID NO:52 (HtH2 domain d'), SEQ ID NO:53 (HtH2 domain e'), SEQ ID NO:54 (KLH1 domain e'), SEQ ID NO:55 (KLH1 domain f), SEQ ID NO:56 (KLH1 domain g), SEQ ID NO:57 (KLH2 domain b'), SEQ ID NO:58 (KLH2 domain c'), SEQ ID NO:59 (KLH2 domain d'), SEQ ID NO:60 (KLH2 domain e),

SEQ ID NO:61 (KLH2 domain f),

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SEO ID NO:62 (KLH2 domain g!)

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SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtHl domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
SEQ ID NO:108 (partial KLH2 domain h");
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- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences described under (a) to (f).

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- 17. Process according to claim 16, characterized in that the haemocyanin polypeptide prepared is modified naturally or chemically.
- 18. Process according to claim 17, characterized in that the modification is a crosslinking or a covalent bonding to an antigen.
- 19. Process according to one of claims 16 to 18, characterized in that the expression is carried out in a host cell according to one of claims 13 to 15.
- 20. Haemocyanin polypeptide, comprising an amino acid sequence which is coded by one or more of athe nucleic acid molecules— comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:
- (b) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),

SEQ ID NO:2 (HtH1 domain b),

SEQ ID NO:3 (HtH1 domain c),

SEQ ID NO:4 (HtH1 domain d),

SEQ ID NO:5 (HtH1 domain e), SEQ ID NO:6 (HtH1 domain f), SEQ ID NO:7 (HtH1 domain g), SEQ ID NO: 8 (HtH1 domain h), SEQ ID NO:9 (partial HtH2 domain b), SEQ ID NO:10 (HtH2 domain c), SEQ ID NO:11 (HtH2 domain d), SEQ ID NO:12 (HtH2 domain e), SEQ ID NO:13 (HtH2 domain f), SEQ ID NO:14 (HtH2 domain g), SEQ ID NO:15 (HtH2 domain h), SEQ ID NO:16 (partial KLH1 domain b), SEQ ID NO:17 (KLH1 domain c), SEQ ID NO:18 (KLH1 domain d), SEQ ID NO:19 (partial KLH1 domain e), SEQ ID NO:20 (KLH2 domain b), SEQ ID NO:21 (KLH2 domain c), SEQ ID NO:22 (partial KLH2 domain d), SEQ ID NO:23 (KLH2 domain g), SEQ ID NO:24 (partial KLH2 domain h), SEQ ID NO:49 (HtH1 domain a' + signal peptide), SEQ ID NO:50 (partial HtH2 domain a), SEQ ID NO:51 (HtH2 domain b'), SEQ ID NO:52 (HtH2 domain d'), SEQ ID NO:53 (HtH2 domain e'), SEQ ID NO:54 (KLH1 domain e'), SEQ ID NO:55 (KLH1 domain f), SEQ ID NO:56 (KLH1 domain g), SEQ ID NO:57 (KLH2 domain b'), SEQ ID NO:58 (KLH2 domain c'),

SEQ ID NO:59 (KLH2 domain d'),

Preliminary Amendment -20showing changes for § 371 Patent Application of PCT/EP00/02410 Markl, et al. filed September 17, 2001 SEQ ID NO:60 (KLH2 domain e), SEQ ID NO:61 (KLH2 domain f), SEQ ID NO:62 (KLH2 domain g'), SEQ ID NO:80 (HtH1 domain a" + signal peptide), SEQ ID NO:81 (HtH1 domain b"), SEQ ID NO:82 (HtH1 domain c"), SEQ ID NO:83 (HtH1 domain d"), SEQ ID NO:84 (HtH1 domain e"), SEQ ID NO:85 (HtH1 domain f"), SEQ ID NO:86 (HtH1 domain g"), SEQ ID NO:87 (HtH1 domain h"), SEQ ID NO:88 (partial HtH2 domain a"), SEQ ID NO:89 (HtH2 domain b"), SEQ ID NO:90 (HtH2 domain c"), SEQ ID NO:91 (HtH2 domain d"), SEQ ID NO:92 (HtH2 domain e"), SEQ ID NO:93 (HtH2 domain f"), SEQ ID NO:94 (HtH2 domain g"), SEQ ID NO:95 (HtH2 domain h"), SEQ ID NO:96 (partial KLH1 domain b"), SEQ ID NO:97 (KLH1 domain c"), SEQ ID NO:98 (KLH1 domain d"), SEQ ID NO:99 (KLH1 domain e"), SEQ ID NO:100 (KLH1 domain f"), SEQ ID NO:101 (KLH1 domain g"), SEQ ID NO:102 (KLH2 domain b"), SEQ ID NO:103 (KLH2 domain c"), SEQ ID NO:104 (KLH2 domain d"), SEQ ID NO:105 (KLH2 domain e"), SEQ ID NO:106 (KLH2 domain f"),

SEQ ID NO:107 (KLH2 domain g"),

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SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and

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showing changes for
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- (g) combinations of several of the DNA sequences described under (a) to (f) according to one of claims 1 to 6.
- 21. Haemocyanin polypeptide according to claim 20, comprising at least one amino acid sequence selected from the following group:

```
SEQ ID NO:25 (HtH1 domain a + signal peptide),
SEQ ID NO:26 (HtH1 domain b),
SEQ ID NO:27 (HtH1 domain c),
SEQ ID NO:28 (HtH1 domain d),
SEQ ID NO:29 (HtH1 domain e),
SEQ ID NO:30 (HtH1 domain f),
SEQ ID NO:31 (HtH1 domain g),
SEQ ID NO:32 (HtH1 domain h),
SEQ ID NO:33 (partial HtH2 domain b),
SEQ ID NO:34 (HtH2 domain c),
SEQ ID NO:35 (HtH2 domain d),
SEQ ID NO:36 (HtH2 domain e),
SEQ ID NO:37 (HtH2 domain f),
SEQ ID NO:38 (HtH2 domain g),
SEQ ID NO:39 (HtH2 domain h),
SEQ ID NO:40 (partial KLH1 domain b),
SEQ ID NO:41 (KLH1 domain c),
SEQ ID NO:42 (partial KLH1 domain d),
SEQ ID NO:43 (partial KLH1 domain e),
SEQ ID NO:44 (KLH2 domain b),
SEQ ID NO:45 (KLH2 domain c),
SEQ ID NO:46 (partial KLH2 domain d),
SEQ ID NO:47 (KLH2 domain q),
```

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   SEQ ID NO:48 (partial KLH2 domain h),
   SEQ ID NO:63 (HtH1 domain a' + signal peptide),
   SEQ ID NO:64 (HtH1 domain h'),
   SEQ ID NO:65 (partial HtH2 domain a),
   SEQ ID NO:66 (HtH2 domain b'),
   SEQ ID NO:67 (HtH2 domain d'),
   SEQ ID NO:68 (HtH2 domain e'),
   SEQ ID NO:69 (partial KLH1 domain b'),
   SEQ ID NO:70 (KLH1 domain e'),
   SEQ ID NO:71 (KLH1 domain f),
  SEQ ID NO:72 (KLH1 domain q),
  SEQ ID NO:73 (KLH1 domain h),
  SEQ ID NO:74 (KLH2 domain b'),
   SEQ ID NO:75 (KLH2 domain c'),
  SEQ ID NO:76 (KLH2 domain d'),
   SEQ ID NO:77 (KLH2 domain e),
   SEQ ID NO:78 (KLH2 domain f),
  SEQ ID NO:79 (KLH2 domain g'),
```

or a fragment of one of these sequences which has the immunological properties of at least one domain of a haemocyanin.

22. Recombinant haemocyanin polypeptide, obtainable by athe process for the preparation of a haemocyanin polypeptide, wherein a nucleic acid molecule and/or a construct comprising said nucleic acid molecule is expressed in a suitable host cell and the protein is isolated, if appropriate, wherein said nucleic acid molecule comprising a nucleic acid molecule comprises a nucleic acid sequence which codes for a

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haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(b) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

```
SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
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SEQ ID NO:20 (KLH2 domain b), SEQ ID NO:21 (KLH2 domain c),

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   SEQ ID NO:22 (partial KLH2 domain d),
   SEQ ID NO:23 (KLH2 domain g),
   SEQ ID NO:24 (partial KLH2 domain h),
   SEQ ID NO:49 (HtHl domain a' + signal peptide),
   SEQ ID NO:50 (partial HtH2 domain a),
   SEQ ID NO:51 (HtH2 domain b'),
   SEQ ID NO:52 (HtH2 domain d'),
   SEQ ID NO:53 (HtH2 domain e'),
   SEQ ID NO:54 (KLH1 domain e'),
   SEQ ID NO:55 (KLH1 domain f),
   SEQ ID NO:56 (KLH1 domain g),
   SEQ ID NO:57 (KLH2 domain b'),
   SEQ ID NO:58 (KLH2 domain c'),
   SEQ ID NO:59 (KLH2 domain d'),
   SEQ ID NO:60 (KLH2 domain e),
   SEQ ID NO:61 (KLH2 domain f),
   SEQ ID NO:62 (KLH2 domain g'),
   SEQ ID NO:80 (HtH1 domain a" + signal peptide),
   SEQ ID NO:81 (HtHl domain b"),
   SEQ ID NO:82 (HtH1 domain c"),
   SEQ ID NO:83 (HtH1 domain d"),
   SEQ ID NO:84 (HtH1 domain e"),
   SEQ ID NO:85 (HtH1 domain f"),
   SEQ ID NO:86 (HtH1 domain g"),
   SEQ ID NO:87 (HtH1 domain h"),
   SEQ ID NO:88 (partial HtH2 domain a"),
   SEQ ID NO:89 (HtH2 domain b"),
   SEQ ID NO:90 (HtH2 domain c"),
   SEQ ID NO:91 (HtH2 domain d"),
   SEQ ID NO:92 (HtH2 domain e"),
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SEQ ID NO:93 (HtH2 domain f"),

SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain d"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain f"),

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties

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of at least one domain of a haemocyanin;

- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences

 described under (a) to (f) according to one of claims

 16 to 19 or modifications thereof.
- 23. Recombinant haemocyanin polypeptide according to claim 22, characterized in that it comprises the sequences SEQ ID NO: 25 to 32 and is haemocyanin 1 from Haliotis tuberculata, it being possible for the sequence with SEQ ID NO:25 to be replaced by SEQ ID NO:63 and/or SEQ ID NO:32 to be replaced by SEQ ID NO:64.
- 24. Recombinant haemocyanin polypeptide according to claim 22, characterized in that it comprises either the sequences SEQ ID NO: 33 to 39 or the sequences SEQ ID NO:65, 66, 34-39 and is haemocyanin 2 from Haliotis tuberculata, it being possible in each case

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for SEQ ID NO:35 to be replaced by SEQ ID NO:67 and/or SEQ ID NO:36 to be replaced by SEQ ID NO:68.

- 25. Recombinant haemocyanin polypeptide according to claim 23, characterized in that it has an apparent molecular weight of 370 kDa in SDS-PAGE under reducing conditions.
- 26. Recombinant haemocyanin polypeptide according to claim 24, characterized in that it has an apparent molecular weight of 370 kDa in SDS-PAGE under reducing conditions.
- 27. Recombinant haemocyanin polypeptide according to claim 21, characterized in that the haemocyanin polypeptide comprises either the sequences SEQ ID NO: 40 to 43 or the sequences SEQ ID NO:40 to 43 and SEQ ID NO:71 to 73 and is KLH1 from Megathura crenulata, it being possible in each case the for sequence with SEQ ID NO:40 to be replaced by SEQ ID NO:66 and/or SEQ ID NO:43 to be replaced by SEQ ID NO:70.
- 28. Recombinant haemocyanin polypeptide according to claim 21, characterized in that the haemocyanin polypeptide comprises either the sequences SEQ ID NO: 44 to 48 or the sequences SEQ ID NO:44 to 46, 77, 78, 47, 48 and is KLH2 from Megathura crenulata, in being possible in each case for the sequence with SEQ ID NO:44 to be replaced by SEQ ID NO:74, SEQ ID NO:45 to be replaced by SEQ ID NO:75, SEQ ID NO:46 to be replaced by SEQ ID NO:76 and/or SEQ ID NO:47 to be

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replaced by SEQ ID NO:79.

- 29. Recombinant haemocyanin polypeptide according to one of claims 20—to 28, characterized in that it is bonded covalently to viruses, virus constituents, bacteria, bacteria constituents, DNA, DNA constituents, inorganic or organic molecules, such as e.g. carbohydrates, peptides and/or glycoproteins.
- 30. Recombinant haemocyanin polypeptide according to one of claims 20 to 29, characterized in that the haemocyanin polypeptide is non-glycosylated.
- 31. Recombinant haemocyanin polypeptide according to one of claims 20 to 29, characterized in that the haemocyanin polypeptide is glycosylated.
- 32. Pharmaceutical composition, comprising a nucleic acid molecule according to one of claims 1 to 6 and/or a construct comprising said nucleic acid moleculeaccording to one of claims 7 to 12 and physiologically tolerated additives, wherein said nucleic acid molecule comprises a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:
- (b) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown

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below or the corresponding RNA sequences or which contain these:

```
SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtHl domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
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SEQ ID NO:52 (HtH2 domain d'),

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SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
*SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
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SEQ ID NO:101 (KLH1 domain g"),

SEQ ID NO:102 (KLH2 domain b"),

SEQ ID NO:103 (KLH2 domain c"),

SEQ ID NO:104 (KLH2 domain d"),

SEQ ID NO:105 (KLH2 domain e"),

SEQ ID NO:106 (KLH2 domain f"),

SEQ ID NO:107 (KLH2 domain g"),

SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerate to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one
 of the nucleic acid sequences described under (a)
 to (c) and the counter-strand of which codes for a
 polypeptide which has the immunological properties
 of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to

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- (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences described under (a) to (f).
- 33. Pharmaceutical composition according to claim32, characterized in that it is used for gene therapy treatment of tumours.
- 34. Pharmaceutical composition, comprising a haemocyanin polypeptide according to one of claims 20 to 31 and physiologically tolerated additives, wherein said haemocyanin polypeptide comprises an amino acid sequence which is coded by one or more of the nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:
- (b) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

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   SEQ ID NO:1 (HtH1 domain a + signal peptide),
   SEQ ID NO:2 (HtH1 domain b),
   SEQ ID NO:3 (HtH1 domain c),
   SEQ ID NO:4 (HtH1 domain d),
   SEQ ID NO:5 (HtH1 domain e),
   SEQ ID NO:6 (HtH1 domain f),
   SEQ ID NO:7 (HtH1 domain g),
   SEQ ID NO: 8 (HtH1 domain h),
   SEQ ID NO:9 (partial HtH2 domain b),
   SEQ ID NO:10 (HtH2 domain c),
   SEQ ID NO:11 (HtH2 domain d),
   SEQ ID NO:12 (HtH2 domain e),
   SEQ ID NO:13 (HtH2 domain f),
   SEQ ID NO:14 (HtH2 domain g),
```

SEQ ID NO:17 (KLH1 domain c),

SEQ ID NO:15 (HtH2 domain h),

SEQ ID NO:18 (KLH1 domain d),

SEQ ID NO:19 (partial KLH1 domain e),

SEQ ID NO:16 (partial KLH1 domain b),

SEQ ID NO:20 (KLH2 domain b),

SEQ ID NO:21 (KLH2 domain c),

SEQ ID NO:22 (partial KLH2 domain d),

SEQ ID NO:23 (KLH2 domain g),

SEQ ID NO:24 (partial KLH2 domain h),

SEQ ID NO:49 (HtH1 domain a' + signal peptide),

SEQ ID NO:50 (partial HtH2 domain a),

SEQ ID NO:51 (HtH2 domain b'),

SEQ ID NO:52 (HtH2 domain d'),

SEQ ID NO:53 (HtH2 domain e'),

SEQ ID NO:54 (KLH1 domain e'),

SEQ ID NO:55 (KLH1 domain f),

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```
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
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SEQ ID NO:103 (KLH2 domain c"),

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SEQ ID NO:104 (KLH2 domain d"),

SEQ ID NO:105 (KLH2 domain e"),

SEQ ID NO:106 (KLH2 domain f"),

SEQ ID NO:107 (KLH2 domain g"),

SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding

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for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and

- (g) combinations of several of the DNA sequences described under (a) to (f).
- 35. Pharmaceutical composition according to claim 34, characterized in that it is used as an antiparasitic composition, antivirus composition or as an antitumour composition.
- 36. Pharmaceutical composition according to claim 34, characterized in that it is used for treatment of one of the following diseases: _schistosomiasis, high blood pressure, surface bladder carcinomas, epithelial carcinomas, ovarian carcinoma, mammary carcinoma, bronchial carcinoma and colorectal carcinoma.
- 37. Pharmaceutical composition according to claim
- 34, characterized in that it is used as a vaccine.
- 38. Pharmaceutical composition according to claim
- 34, characterized in that it is used for prevention of cocaine abuse.
- 39. Use of a haemocyanin polypeptide according to one of claims 20 to 31 as a carrier substance for medicaments, wherein said haemocyanin polypeptide comprises an amino acid sequence which is coded by

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one or more of the nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(b) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

```
SEQ ID NO:1 (HtH1 domain a + signal peptide),
   SEQ ID NO:2 (HtH1 domain b),
  SEQ ID NO:3 (HtH1 domain c),
  SEQ ID NO:4 (HtH1 domain d),
  SEQ ID NO:5 (HtH1 domain e),
  SEQ ID NO:6 (HtH1 domain f),
  SEQ ID NO:7 (HtH1 domain g),
  SEQ ID NO: 8 (HtH1 domain h),
  SEQ ID NO:9 (partial HtH2 domain b),
  SEQ ID NO:10 (HtH2 domain c),
  SEQ ID NO:11 (HtH2 domain d),
  SEQ ID NO:12 (HtH2 domain e),
  SEQ ID NO:13 (HtH2 domain f),
  SEQ ID NO:14 (HtH2 domain g),
  SEQ ID NO:15 (HtH2 domain h),
  SEQ ID NO:16 (partial KLH1 domain b),
  SEQ ID NO:17 (KLH1 domain c),
  SEQ ID NO:18 (KLH1 domain d),
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SEQ ID NO:19 (partial KLH1 domain e),

Preliminary Amendment -39showing changes for § 371 Patent Application of PCT/EP00/02410 Markl, et al. filed September 17, 2001 SEQ ID NO:20 (KLH2 domain b), SEQ ID NO:21 (KLH2 domain c), SEQ ID NO:22 (partial KLH2 domain d), SEQ ID NO:23 (KLH2 domain g), SEQ ID NO:24 (partial KLH2 domain h), SEQ ID NO:49 (HtH1 domain a' + signal peptide), SEQ ID NO:50 (partial HtH2 domain a), SEQ ID NO:51 (HtH2 domain b'), SEQ ID NO:52 (HtH2 domain d'), SEQ ID NO:53 (HtH2 domain e'), SEQ ID NO:54 (KLH1 domain e'), SEQ ID NO:55 (KLH1 domain f), SEQ ID NO:56 (KLH1 domain g), SEQ_ID_NO:57 (KLH2 domain b'), SEQ ID NO:58 (KLH2 domain c'), SEQ ID NO:59 (KLH2 domain d'), SEQ ID NO:60 (KLH2 domain e), SEQ ID NO:61 (KLH2 domain f), SEQ ID NO:62 (KLH2 domain g'), SEQ ID NO:80 (HtH1 domain a" + signal peptide), SEQ ID NO:81 (HtH1 domain b"), SEQ ID NO:82 (HtH1 domain c"), SEQ ID NO:83 (HtH1 domain d"), SEQ ID NO:84 (HtH1 domain e"), SEQ ID NO:85 (HtH1 domain f"), SEQ ID NO:86 (HtH1 domain g"), SEQ ID NO:87 (HtH1 domain h"), SEQ ID NO:88 (partial HtH2 domain a"), SEQ ID NO:89 (HtH2 domain b"), SEQ ID NO:90 (HtH2 domain c"),

SEQ ID NO:91 (HtH2 domain d"),

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SEQ ID NO:92 (HtH2 domain e"), SEQ ID NO:93 (HtH2 domain f"), SEQ ID NO:94 (HtH2 domain g"), SEQ ID NO:95 (HtH2 domain h"), SEQ ID NO:96 (partial KLH1 domain b"), SEQ ID NO:97 (KLH1 domain c"), SEQ ID NO:98 (KLH1 domain d"), SEQ ID NO:99 (KLH1 domain e"), SEQ ID NO:100 (KLH1 domain f"), SEQ ID NO:101 (KLH1 domain q"), SEQ ID NO:102 (KLH2 domain b"), SEQ ID NO:103 (KLH2 domain c"), SEQ ID NO:104 (KLH2 domain d"), SEQ ID NO:105 (KLH2 domain e"), SEQ ID NO:106 (KLH2 domain f"), SEQ ID NO:107 (KLH2 domain g"), SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a)

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- to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences described under (a) to (f).
- 40. Liposome, comprising a nucleic acid molecule according to one of claims 1 to 6, a construct comprising said nucleic acid molecule according to one of claims 7 to 12 and/or a haemocyanin polypeptide encoded by said nucleic acid molecule according to one of claims 20 to 31, wherein said nucleic acid molecule comprises a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

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(b) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

```
SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain q),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
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SEQ ID NO:50 (partial HtH2 domain a),

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SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
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SEQ ID NO:99 (KLH1 domain e"),

SEQ ID NO:100 (KLH1 domain f"),

SEQ ID NO:101 (KLH1 domain g"),

SEQ ID NO:102 (KLH2 domain b"),

SEQ ID NO:103 (KLH2 domain c"),

SEQ ID NO:104 (KLH2 domain d"),

SEQ ID NO:105 (KLH2 domain e"),

SEQ ID NO:106 (KLH2 domain f"),

SEQ ID NO:107 (KLH2 domain g"),

SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerate to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);

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- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences described under (a) to (f).
- 41. Liposome according to claim 40, characterized in that the liposome furthermore comprises cell recognition molecules.
- 42. Antibodies, obtainable by immunization of a test animal with athe recombinant haemocyanin polypeptide comprising an amino acid sequence which is coded by one or more of the nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:
- (b) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

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SEQ ID NO:1 (HtH1 domain a + signal peptide), SEQ ID NO:2 (HtH1 domain b), SEQ ID NO:3 (HtH1 domain c), SEQ ID NO:4 (HtH1 domain d), SEQ ID NO:5 (HtHl domain e), SEQ ID NO:6 (HtH1 domain f), SEQ ID NO:7 (HtH1 domain g), SEQ ID NO: 8 (HtH1 domain h), SEQ ID NO:9 (partial HtH2 domain b), SEQ ID NO:10 (HtH2 domain c), SEQ ID NO:11 (HtH2 domain d), SEQ ID NO:12 (HtH2 domain e), SEQ ID NO:13 (HtH2 domain f), SEQ ID NO:14 (HtH2 domain g), SEQ ID NO:15 (HtH2 domain h), SEQ ID NO:16 (partial KLH1 domain b), SEQ ID NO:17 (KLH1 domain c), SEQ ID NO:18 (KLH1 domain d), SEQ ID NO:19 (partial KLH1 domain e), SEQ ID NO:20 (KLH2 domain b), SEQ ID NO:21 (KLH2 domain c), SEQ ID NO:22 (partial KLH2 domain d), SEQ ID NO:23 (KLH2 domain g), SEQ ID NO:24 (partial KLH2 domain h), SEQ ID NO:49 (HtH1 domain a' + signal peptide), SEQ ID NO:50 (partial HtH2 domain a), SEQ ID NO:51 (HtH2 domain b'), SEQ ID NO:52 (HtH2 domain d'), SEQ ID NO:53 (HtH2 domain e'), SEQ ID NO:54 (KLH1 domain e'), SEQ ID NO:55 (KLH1 domain f),

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SEQ ID NO:56 (KLH1 domain g), SEQ ID NO:57 (KLH2 domain b'), SEQ ID NO:58 (KLH2 domain c'), SEQ ID NO:59 (KLH2 domain d'), SEQ ID NO:60 (KLH2 domain e), SEQ ID NO:61 (KLH2 domain f), SEQ ID NO:62 (KLH2 domain g'), SEQ ID NO:80 (HtH1 domain a" + signal peptide), SEQ ID NO:81 (HtH1 domain b"), SEQ ID NO:82 (HtH1 domain c"), SEQ ID NO:83 (HtH1 domain d"), SEQ ID NO:84 (HtHl domain e"), SEQ ID NO:85 (HtH1 domain f"), SEQ ID NO:86 (HtH1 domain g"), SEQ ID NO:87 (HtH1 domain h"), SEQ ID NO:88 (partial HtH2 domain a"), SEQ ID NO:89 (HtH2 domain b"), SEQ ID NO:90 (HtH2 domain c"), SEQ ID NO:91 (HtH2 domain d"), SEQ ID NO:92 (HtH2 domain e"), SEQ ID NO:93 (HtH2 domain f"), SEQ ID NO:94 (HtH2 domain g"), SEQ ID NO:95 (HtH2 domain h"), SEQ ID NO:96 (partial KLH1 domain b"), SEQ ID NO:97 (KLH1 domain c"), SEQ ID NO:98 (KLH1 domain d"), SEQ ID NO:99 (KLH1 domain e"), SEQ ID NO:100 (KLH1 domain f"), SEQ ID NO:101 (KLH1 domain g"), SEQ ID NO:102 (KLH2 domain b"),

SEQ ID NO:103 (KLH2 domain c"),

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SEQ ID NO:104 (KLH2 domain d"),

SEQ ID NO:105 (KLH2 domain e"),

SEQ ID NO:106 (KLH2 domain f"),

SEQ ID NO:107 (KLH2 domain g"),

SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to
 (d), the variants containing additions, deletions,
 insertions or inversions with respect to the
 sequences described under (a) to (d) and coding

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for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and

- (g) combinations of several of the DNA sequences described under (a) to (f) according to one of claims 20 to 31.
- 43. Screening method for identification of tumourspecific DNA in a cell, comprising:
- A.a) bringing cell DNA and/or cell protein into contact with a probe comprising athe nucleic acid moleculesequence according to one of claims 1 to 6 and/or the antibody obtainable by immunization of a test animal with a recombinant haemocyanin polypeptide comprising an amino acid sequence which is coded by one or more of said nucleic acid molecules, wherein said nucleic acid molecule comprises a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:
- (b) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),

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SEQ ID NO:3 (HtH1 domain c), SEQ ID NO:4 (HtH1 domain d), SEQ ID NO:5 (HtH1 domain e), SEQ ID NO:6 (HtH1 domain f), SEQ ID NO:7 (HtH1 domain g), SEQ ID NO: 8 (HtH1 domain h), SEQ ID NO:9 (partial HtH2 domain b), SEQ ID NO:10 (HtH2 domain c), SEQ ID NO:11 (HtH2 domain d), SEQ ID NO:12 (HtH2 domain e), SEQ ID NO:13 (HtH2 domain f), SEQ ID NO:14 (HtH2 domain g), SEQ ID NO:15 (HtH2 domain h), SEQ ID NO:16 (partial KLH1 domain b), SEQ ID NO:17 (KLH1 domain c), SEQ ID NO:18 (KLH1 domain d), SEQ ID NO:19 (partial KLH1 domain e), SEQ ID NO:20 (KLH2 domain b), SEQ ID NO:21 (KLH2 domain c), SEQ ID NO:22 (partial KLH2 domain d), SEQ ID NO:23 (KLH2 domain g), SEQ ID NO:24 (partial KLH2 domain h), SEQ ID NO:49 (HtH1 domain a' + signal peptide), SEQ ID NO:50 (partial HtH2 domain a), SEQ ID NO:51 (HtH2 domain b'), SEQ ID NO:52 (HtH2 domain d'), SEQ ID NO:53 (HtH2 domain e'), SEQ ID NO:54 (KLH1 domain e'), SEQ ID NO:55 (KLH1 domain f), SEQ ID NO:56 (KLH1 domain g), SEQ ID NO:57 (KLH2 domain b'),

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   SEQ ID NO:58 (KLH2 domain c'),
   SEQ ID NO:59 (KLH2 domain d'),
   SEQ ID NO:60 (KLH2 domain e),
   SEQ ID NO:61 (KLH2 domain f),
   SEQ ID NO:62 (KLH2 domain g'),
   SEQ ID NO:80 (HtH1 domain a" + signal peptide),
   SEQ ID NO:81 (HtH1 domain b"),
   SEQ ID NO:82 (HtH1 domain c"),
   SEQ ID NO:83 (HtH1 domain d"),
   SEQ ID NO:84 (HtH1 domain e"),
   SEQ ID NO:85 (HtH1 domain f"),
   SEQ ID NO:86 (HtH1 domain g"),
   SEQ ID NO:87 (HtH1 domain h"),
   SEQ ID NO:88 (partial HtH2 domain a"),
   SEQ ID NO:89 (HtH2 domain b"),
   SEQ ID NO:90 (HtH2 domain c"),
   SEQ ID NO:91 (HtH2 domain d"),
   SEQ ID NO:92 (HtH2 domain e"),
   SEQ ID NO:93 (HtH2 domain f"),
   SEQ ID NO:94 (HtH2 domain g"),
   SEQ ID NO:95 (HtH2 domain h"),
   SEQ ID NO:96 (partial KLH1 domain b"),
   SEQ ID NO:97 (KLH1 domain c"),
   SEQ ID NO:98 (KLH1 domain d"),
   SEQ ID NO:99 (KLH1 domain e"),
   SEQ ID NO:100 (KLH1 domain f"),
   SEQ ID NO:101 (KLH1 domain g"),
   SEQ ID NO:102 (KLH2 domain b"),
   SEQ ID NO:103 (KLH2 domain c"),
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SEQ ID NO:104 (KLH2 domain d"), SEQ ID NO:105 (KLH2 domain e"), Preliminary Amendment -52showing changes for § 371 Patent Application of PCT/EP00/02410 Markl, et al. filed September 17, 2001

SEQ ID NO:106 (KLH2 domain f"),

SEQ ID NO:107 (KLH2 domain g"),

SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin;

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and

- (g) combinations of several of the DNA sequences

 described under (a) to (f) according to claim 42 and

 B. b) detecting the specific binding.
- 44. Screening method according to claim
 43, characterized in that the tumour to be detected
 is a bladder carcinoma, epithelial carcinoma, ovarian
 carcinoma, mammary carcinoma, bronchial carcinoma or
 colorectal carcinoma.